## REMARKS

Claims 31-33 are pending in this application. No Claims have been a

**Double Patenting Rejection**

Claim 31 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over Claim 1 of copending Application No. 10/427,929 (the "Copending '929 Application").

It is respectfully requested that this issue be deferred until allowable subject matter is indicated.

**Rejection Under 35 USC §102**

Claims 31-33 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Kolb et al., *Life Sciences*, **1991**, *49*(25), PL213-PL217, (the "Kolb et al. reference") or Pizcutea et al. *Gastroenterology*, **1992**, *103*(6), 1909-1915 (the "Pizcutea et al. reference"). Specifically, the Office Action states that these two "references, each individually, teach the administration of a nitric oxide synthase inhibitor to treat diseases or disorders resulted from reduced α1-antitrypsin activity as described in applicants' specification.... Inherently, the levels of α1-trypsin in the tissue are spared by inhibitors that suppress nitric oxide synthesis...since the inhibitors are known to posses α1-antitrypsin [sic] activity." Page 5 of the Office Action.

As will be recognized, claims are anticipated if, and only if, **each and every element** as set forth in the claim is found in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051 (Fed. Cir. 1989). Furthermore, "[t]he **identical invention must be shown in as complete detail as is contained in the...claim**." (emphasis added) *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913 (Fed. Cir. 1989). See also, *PPG Industries Inc. v. Guardian Industries Corp.*, 7 USPQ2d 1618, 1624 (Fed. Cir. 1996) ("To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.")

It is also well known that there are many different modes of developing any particular disease. For example, cancer can result from radiation exposure, viral infection, chemical exposure, genetic susceptibility, etc.

The Kolb et al. reference discusses using "low dose **streptozotocin induced diabetes** [mouse] model" to show that N-nitro-L-argininemethylester [NAME] partially suppresses diabetes development. (Emphasis added). See the abstract provide by the Examiner. As stated in the Kolb et al. reference, the mouse model used in the Kolb et al. is treated with **the low dose streptozotocin to induce diabetes**. Diabetes development in these mouse models has nothing to do with the α1-antitrypsin level. Accordingly, it is submitted that the Kolb et al. reference discusses using NAME to partially suppress diabetes development caused by a low dose of streptozotocin. This mode of diabetes development is different from that contemplated in the present application as well as the Copending '929 Application, which require clinical conditions caused by α1-antitrypsin level not by administration of a low dose of streptozotocin.

The Pizcueta et al. reference discusses investigating the effects of $N^G$-monomethyl-L-arginine (L-NMMA) "in rats with **cirrhosis induced by carbon tetrachloride**". (Emphasis added). See the first sentence of the Abstract provided by the Examiner. The Abstract then goes on to discuss that in rats with cirrhosis induced by carbon tetrachloride "local excess formation of NO contributes to changes in splanchnic circulation associated with portal hypertension in cirrhosis." *Id.* Thus, cirrhosis of the rats in the Pizcueta et al. reference is a result of exposure to carbon tetrachloride not due to the level of α1-antitrypsin. Accordingly, it is submitted that causation of cirrhosis in rats of the Pizcueta et al. reference is different from that contemplated in the present application, which is caused by the decreased level of α1-antitrypsin.

As discussed above, the clinical conditions manifested in the mice in the Kolb et al. reference and the rats in the Pizcueta et al. reference are results of administration of external chemicals (e.g., streptozotocin in the Kolb et al. reference and carbon tetrachloride in the Pizcueta et al. reference). There is nothing in these references to indicate that the clinical conditions are due to change in α1-antitrypsin levels. Since diabetes and cirrhosis have many causes of manifestation (for example, diabetes can be due to genetic defect, obesity, death of islet cells by infection or chemical exposure and cirrhosis can be due to excessive alcohol consumption, drug abuse, viral infection of liver, etc.), the implied assertion in the Office Action that clinical conditions discussed in rats and mice of the Pizcueta et al. reference and the Kolb et al. reference, respectively, are due to decrease in α1-antitrypsin level is without merit. In fact, since the clinical conditions in the rats and mice of the Pizcueta et al. reference and the Kolb et al.

reference, respectively, are due to exposure to chemicals, it is likely that the α1-antitrypsin levels in these rats and mice are not different from rats and mice that were not exposed to these chemicals. In contrast, Claims of the present invention are directed to sparing tissue levels of α1-antitrypsin in an animal. Thus, it is submitted that without a reasonable basis to show that the clinical conditions discussed in the Pizcueta et al. reference and the Kolb et al. reference are due to decreased α1-antitrypsin activity level and not to the exposure to the external chemicals, rejection under 35 U.S.C. §102(b) is improper.

Accordingly, it is respectfully submitted that the rejection of Claims 31-33 under 35 U.S.C. §102(b) be withdrawn.

## CONCLUSION

In view of the foregoing, it is respectfully submitted that all claims now pending in this Application are in condition for allowance. Therefore, an early Office Action to that effect is earnestly solicited. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at (303) 955-8103.

Respectfully submitted,

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